

A Cross-Sectional Study of Clinical and Immunological Profile of SLE Patients from a Tertiary Care Center in the Sub Himalayan Region of Northern India

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ABSTRACT

Introduction: Systemic Lupus Erythematosus (SLE) is a disease of thousand faces whose manifestations vary with the interplay of genetic, ethnic, and host factors along with environmental exposures and geographical conditions. Since the first case of SLE reported in India in 1955, many case series have been published from various centers depicting Clinical and Immunological features in the Indian population. This study was undertaken to study the clinical and immunological profile in a tertiary care center in the sub-Himalayan region of northern India.

Materials and Methods: This study is a cross-sectional retrospective study conducted at a tertiary care center in the hilly northern state of Himachal Pradesh over a period of 1 year; from 1st June 2017 to 31st May 2018. The records of all patients admitted in the study period with the department of medicine and diagnosed with SLICC 2012 classification criteria were studied to abstract the Clinical and Immunological profile of patients.

Results: A total of sixty-nine patients were included in the study. 96% of the subjects were female patients, and 84% of the patients were in the reproductive age group of 20-40 years. Mucocutaneous manifestations were most commonly seen in nearly 89% of patients followed by musculoskeletal involvement in

about 71%. Hematological involvement was more frequent than reported in the literature. Lupus Nephritis was diagnosed in about 30 % of the patients. Fatigue and synovitis were the most common features, followed by oral ulcers and acute cutaneous lupus. ANA and ds DNA positivity was 98.5 and 72.4 % respectively. Six cases of MCTD were found in the study group.

Conclusion: In hospitalized SLE patients admitted in a tertiary care center of the northern hilly state, females of reproductive age group constituted the majority of patients. Mucocutaneous, Musculoskeletal, hematological, and renal involvement were most prevalent.

Key Words: SLE, cross-sectional study, Mucocutaneous involvement, Renal Biopsy, Hilly area

INTRODUCTION

Systemic Lupus Erythematosus (SLE) is an enigmatic disorder aptly called "disease of thousand faces." It has varied clinical and laboratory manifestations with a plethora of autoantibodies. SLE has marked individual, ethnic, and geographical variations in the presentation and involvement of various organ systems. Outcomes also vary according to ethnicity and socioeconomic status.

The first case of SLE was reported in India in 1955.¹ Prevalence was said to be

3.2/100000 of the population in rural area-based study done in 1993.² Indeed this prevalence is quite low if compared to the Indian migrants settled in other countries. While in epidemiological studies throughout the Asian continent, prevalence rates ranging from 4.3 to 43.5 per 100 000 of the population have been reported.³ Given the variation in available information about the epidemiology of lupus in Asia, a concerted effort using standardized methods will be useful in providing clinically useful and relevant information about how the disease impacts in the region.

Various Indian studies have been published depicting the clinical and immunological profile of SLE patients in the Indian population.^{4,5,6,7,8,9} This study was undertaken to find the clinical and immunological profile of patients afflicted with SLE in the sub-Himalayan region of northern India at an altitude of 3000 meters above sea level.

MATERIAL AND METHODS

Setting:

This study was conducted in Indira Gandhi Medical College, Shimla; a 700 bedded tertiary care center in the hilly state of Himachal Pradesh at an altitude of 3000 meters above sea level.

All the patients admitted with the diagnosis of SLE under the department of Medicine during the study period of 1st June 2017 to 31st May 2018 were included in the study.

Data Collection

The data were obtained retrospectively. A list of patients discharged with the diagnosis of SLE, as per SLICC classification criteria 2012,¹⁰ during the study period was obtained from hospital records. All the data pertaining to the study was analyzed from the hospital records, including demographic, clinical, laboratory, and immunological parameters. Approval from the Institutional Ethics Committee was taken, and no personal data of patients were included in the study.

Analysis

Descriptive analysis of demographic, clinical, laboratory and immunological variables were done. The cumulative percentage frequency of selected variables was calculated using Epi Info software version 7.2.2.

RESULTS

Out of the Sixty-nine patients of SLE were included in the study, 95.65%(66) were females. The mean age for the onset of SLE was 30.5 years. 84.06% of patients were in the reproductive age group of 20-40 years. Most prevalent clinical manifestations were fatigue (78.26%), Oral Ulcers (72.46%), Arthralgias (71.01%), acute cutaneous rash (56.52%) and photosensitivity (43.48%). The most commonly involved system in the decreasing frequency was Mucocutaneous, Musculoskeletal, Haematological, and renal, with a cumulative percentage frequency of 89 %, 71 %, 65 %, and 37.6 % respectively.

Table 1. Mucocutaneous manifestations

	No. of patients	%
Acute Cutaneous Rash	39	56.52
Chronic lupus	6	8.70
Photosensitivity	30	43.48
Oral Ulcers	50	72.46
Alopecia	27	39.13
Livedo reticularis	1	1.45

Table 2. Rheumatological manifestations

	No. of patients	%
Fatigue	54	78.26
Synovitis	49	71.01
Serositis	11	15.94
Raynauds	8	11.59

Table 3 Haematological Manifestations.

	No. of patients	%
Anaemia	52	75.36
Thrombocytopenia	51	73.91
Leucopnea	34	49.28
Autoimmune Anaemia	27	39.13

Table 4. Renal Abnormalities.

	No. of patients	%
Urinary RBC	19	27.54
Urinary CAST	4	5.80
Albuminuria < 500	24	34.78
Albuminuria 30-500	21	30.43
No albuminuria	24	34.78
Biopsy proven Lupus Nephritis	21	30.43

Table 5. Organ system Involvement

	No. of patients	%
Gastrointestinal	1	1.45
Cardiovascular	2	2.90
Neurological	6	8.70
Psychiatric	2	2.90
Pulmonary	7	10.14
Bad Obstetric History	7	10.14
Family History	4	5.80

In mucocutaneous system, Oral Ulcers were most frequent (72.46%) followed by Acute Cutaneous rash (56.5%), Photosensitivity (43.48%), Alopecia (39.13%) and Chronic Lupus (8.7%). Raynaud's phenomenon was present in 11.59% of patients. In musculoskeletal system, joint involvement was

seen in 71.01% of patients. In haematological system, Anaemia was the most common form of involvement seen in 75.6% patients followed by thrombocytopenia (73.9%) and leucopenia (49.2%). Most common renal involvement was in the form of Albuminuria (> 500mg/24hrs) in 34.78% of patients. 27.5% of patients had urinary RBC's while 5.8% had Urinary Casts. 30.43% were diagnosed with Lupus Nephritis on Renal Biopsy. 10.14% of patients had pulmonary involvement in the form of Interstitial Lung Disease and Pulmonary Arterial Hypertension. Frequency of various sign

symptoms and involvement of organ systems is tabulated in Table 1- 6.

Table 6. Autoimmune Profile of study participants.

Auto-antibody	No. of patients	%
ANA	68	98.55
ds DNA	50	72.46
Anti Sm	14	20.29
Anti Ro/La	36	52.7
UI RNP	12	17.39
Anti histone	12	17.39
Anti centromere	7	10.14
scl 70	5	7.25
APLA	3	4.35
C3,C4 low	36	52.17
DCT	27	39.13

Table 7. Comparison of study findings with other studies.

Clinical /immunological Manifestations	Malviya ⁴ (1988) n = 329 (%)	Malviya ⁵ (1997) n = 1366 (%)	Binoy ⁶ (2003) n = 75 (%)	Kosaraju ⁷ (2010) n = 48 (%)	Saigal ⁸ (2011) n = 60 (%)	Agrawal ⁹ (2013) n = 87 (%)	Present study n = 69 (%)
Malar rash	85	58.5	40	35.41	43.3	71.3	56.52
Discoid rash	NA	7	5.3	NA	1.7	32.2	8.7
Alopecia	82	NA	60	18.75	65	10.34	39.13
Oral Ulcer	64	57	64	25	61.7	42.35	72.46
Photosensitivity	67	57	64	25	61.7	42.53	69
Fatigue	NA	NA	NA	NA	NA	NA	78.26
Synovitis	92	85	89.3	64.58	86.7	52.9	71.01
Raynauds	NA	NA	NA	NA	NA	NA	11.59
Hemolytic Anaemia	7	4	1.3	2	25	8.1	39
Leucopenia	16	NA	14.7	NA	43.3	18.4	49.28
Thrombocytopenia	11	9	12	NA	33.3	14.9	73.19
Renal	73	57	33.3	20.83	56.7	69	37.6%
Lupus Nephritis	NA	NA	NA	NA	NA	NA	30.43%
CVS	29	NA	5.3	NA	6.7	2.3	2.9
GIT	NA	NA	NA	NA	NA	NA	1.43
Pulmonary	NA	NA	8	12.5	11.7	12.6	10.14
Neuropsychiatric	38	51	13.3	8.33	13.3	4.6	11.1
ANA	98	97	93.3	64.28	98.3	97.7	98.55
ds DNA	55	68	76	89.36	65	93.9	72.46
ANti Sm	NA	NA	NA	NA	NA	NA	20.29
Anti Ro/La	NA	NA	NA	NA	NA	NA	52.17
UI RNP	NA	NA	NA	NA	NA	NA	17.39
APLA	NA	NA	NA	NA	NA	NA	4.35
No. of MCTD cases	NA	NA	NA	NA	NA	NA	8.7
No. of deaths	NA	NA	NA	NA	NA	NA	5.79

In our study we found one case each of Lupus Enteritis, Acute Lupus Pneumonitis, Conduction heart block and Libmann sack's Endocarditis. One patient was diagnosed with Candidal knee joint arthritis as complication of prolonged immunosuppression. ANA positivity was found in 68 patients (98.55%). One patient was diagnosed with ANA negative SLE on the basis of biopsy-proven Lupus Nephritis. Ds DNA antibodies were seen in 50 patients (72.46 %), followed by Anti Ro/La antibodies in 26 patients (37.68%). APLA were found in 3 patients (4.35 %). Four patients of SLE died in our hospital during the study period. Two of these patients succumbed to Sepsis after receiving Immunosuppression for Lupus Nephritis. The other two deaths were attributed

to Severe PAH leading to RV dysfunction and Cardiogenic shock and Acute lupus Pneumonitis.

DISCUSSION

To the best of our knowledge, this is the first study on SLE from India representing the sub-Himalayan northern Indian population, approximately 3000 meters above the sea level.

In our study, 95 % of the patients were female. In various Indian studies this ranges from 84 -95%.^{4,5,6,8,9,10} Mean age at onset in our study is 30.5 years which is also consistent with other India studies. We had two male patients out of 69 patients. One presented with Synovitis and pericarditis and the other one presented with predominant renal involvement and diagnosed

with Lupus Nephritis. Cumulative Incidence of Mucocutaneous manifestations was 89% in our study, with 62% having cutaneous manifestations in the form of Acute, subacute, or chronic lupus manifestations. 69% of patients with cutaneous involvement had photosensitivity. Dermatological participation in various studies from India varies from 64-85%.^{4,5,6,7,8,9}

Similarly, frequency of acute cutaneous lupus has been ranged from 40-85% in various studies and in the present study we found Acute cutaneous involvement in 56.52% of patients and Chronic Lupus in 8.7%, while chronic lupus has been found to vary from 1-7% in various studies.^{4,5,6,7,8,9} Photosensitivity has been reported in the range of 27-75% in Indian studies and our study photosensitivity was found in 69 % of patients afflicted with cutaneous manifestations. Except in one study from Western India (Saigal et al⁸), Haematological Involvement is seen less frequently in other Indian studies as compared to our study. We had one case of ANA negative SLE proven with renal biopsy and thus ANA positivity rate of 98.5 % with ds DNA and Anti Sm positivity of 72.48 % and 20.29 % consistent with literature.

We had anti-Ro/La antibodies positive in 36 patients. Table 7.

Only three patients with Anti Ro/La positive antibodies were found to have Lupus nephritis, and 22 patients had photosensitivity. This too consistent with the association of Anti Ro/La antibodies, as mentioned in literature. Our study had a few limitations. It was a single retrospective Centre hospital-based study, with a lack of adequate follow-up. Patients with lesser severity of the illness being treated on an outpatient basis have not been represented in this study. A prospective multicenter study is required to confirm the findings of our study.

CONCLUSION

This study shows a high prevalence of Mucocutaneous and Musculoskeletal features in SLE patients consistent with the literature. Our study has higher hematological involvement as compared to other Indian studies. The immunological profile of patients in this study was consistent with that mentioned in the literature. Few rare presentations like Lupus Enteritis, Conduction Heart block, Acute Lupus Pneumonitis were encountered during this study. Ours is probably the first study to document a subset of MCTD cases in SLE

patients. Still, our study doesn't evaluate a representative sample, and thus extensive multicenter and community-based studies are required for accurate depiction of SLE manifestation in our country. Further, Rheumatological disease registries should be set up in Tertiary health care centers for proper follow up and reporting of SLE cases.

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